Welcome to STN International! Enter x:x

LOGINID:SSSPTA1208DXJ

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data

```
 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:07:27 ON 18 JUN 2003

=> eg
EG IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> fil reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:07:33 ON 18 JUN 2003
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   17 JUN 2003  HIGHEST RN 532924-24-6
DICTIONARY FILE UPDATES:  17 JUN 2003  HIGHEST RN 532924-24-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> e verapamil
E1            4     VERANYI/BI
E2            2     VERAP/BI
E3           28 --> VERAPAMIL/BI
E4            2     VERAPAMILAMIDE/BI
E5            2     VERAPAMILIC/BI
E6            1     VERAPAMINE/BI
```
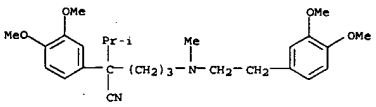

```
E7            1      VERAPATULINE/BI
E8            1      VERAPHEN/BI
E9            1      VERAPHENOL/BI
E10           1      VERAPIN/BI
E11           4      VERAPLI/BI
E12           4      VERAPLIQUIN/BI

=> s e3-e5
             28 VERAPAMIL/BI
              2 VERAPAMILAMIDE/BI
              2 VERAPAMILIC/BI
L1           30 (VERAPAMIL/BI OR VERAPAMILAMIDE/BI OR VERAPAMILIC/BI)

=> e verapamil/cn
E1            1      VERANTHRIDINE, METHIODIDE/CN
E2            1      VERANTIN/CN
E3            1  --> VERAPAMIL/CN
E4            1      VERAPAMIL ALGINATE/CN
E5            1      VERAPAMIL HYDROCHLORIDE/CN
E6            1      VERAPAMIL-CYPROCONAZOLE MIXT./CN
E7            1      VERAPAMIL-PROPICONAZOLE MIXT./CN
E8            1      VERAPAMINE/CN
E9            1      VERAPATULINE/CN
E10           1      VERAPHENOL/CN
E11           1      VERAPIN/CN
E12           1      VERAPLIQUINONE A/CN

=> s e3
L2            1 VERAPAMIL/CN

=> d
```

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 52-53-9 REGISTRY
CN Benzeneacetonitrile,
.alpha.-[3-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino
]propyl]-3,4-dimethoxy-.alpha.-(1-methylethyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Valeronitrile, 5-[(3,4-dimethoxyphenethyl)methylamino]-2-(3,4-
dimethoxyphenyl)-2-isopropyl- (7CI, 8CI)
OTHER NAMES:
CN (.+-.)-Verapamil
CN 5-[(3,4-Dimethoxyphenethyl)methylamino]-2-(3,4-dimethoxy
phenyl)-2-isopropylvaleronitrile
CN CP 16533-1
CN D 365
CN dl-Verapamil
CN Iproveratril
CN NSC 272306NA
CN R,S-Verapamil
CN **Verapamil**
CN VPL
FS 3D CONCORD
DR 7482-85-1, 56949-77-0
MF C27 H38 N2 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
BIOBUSINESS,
BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,
CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE,
HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR,
PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER,
ULIDAT, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

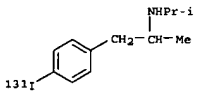


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8147 REFERENCES IN FILE CA (1957 TO DATE)
79 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8159 REFERENCES IN FILE CAPLUS (1957 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> e iodoamphetamine
E1            1      IODOAMPHENICOL/BI
E2            9      IODOAMPHET/BI
E3            9 --> IODOAMPHETAMINE/BI
E4            4      IODOAMYL/BI
E5            1      IODOAMYLATE/BI
E6            1      IODOAMYLDI/BI
E7            1      IODOAMYLDIPROPYL/BI
E8            1      IODOAMYLDIPROPYLTIN/BI
E9            2      IODOAMYLOSE/BI
E10           6      IODOANDROST/BI
E11           1      IODOANDROSTA/BI
E12           2      IODOANDROSTAN/BI

=> s e3
L3            9 IODOAMPHETAMINE/BI

=> d
```

L3 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2003 ACS
RN 91992-07-3 REGISTRY
CN Benzeneethanamine, 4-(iodo-131I)-.alpha.-methyl-N-(1-methylethyl)- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-N-Isopropyl-p-[131I]iodoamphetamine
CN N-Isopropyl-131I-p-iodoamphetamine
CN N-Isopropyl-p-[131I]iodoamphetamine
FS 3D CONCORD
DR 82657-16-7
MF C12 H18 I N
CI COM
LC STN Files: CA, CAPLUS, CASREACT, DRUGPAT, TOXCENTER, USPATFULL



16 REFERENCES IN FILE CA (1957 TO DATE)
16 REFERENCES IN FILE CAPLUS (1957 TO DATE)

```
=> e iodoamphetamine/cn
E1            1      IODOAMMINEBIS(ETHYLENEDIAMINE)PLATINUM TRINITRATE/CN
E2            1      IODOAMPHENICOL/CN
E3            0 --> IODOAMPHETAMINE/CN
E4            1      IODOANILINE/CN
E5            1      IODOANISOLE/CN
E6            1      IODOANTIFEBRIN/CN
E7            1      IODOANTIPYRINE/CN
E8            1      IODOANTIPYRINE-123I/CN
E9            1      IODOAQUOBIS(1,10-PHENANTHROLINE)NICKEL IODIDE/CN
E10           1      IODOAQUOBIS(2,2'-BIPYRIDINE)NICKEL IODIDE/CN
E11           1      IODOAQUOBIS(2,2'-BIPYRIDINE)PLATINUM IODIDE/CN
E12           1      IODOAQUOBIS(2,2'-BIPYRIDINE)PLATINUM PERCHLORATE/CN

=> fil .search
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    25.26      25.47

FILE 'MEDLINE' ENTERED AT 10:08:46 ON 18 JUN 2003

FILE 'CAPLUS' ENTERED AT 10:08:46 ON 18 JUN 2003
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=> d his

     (FILE 'HOME' ENTERED AT 10:07:27 ON 18 JUN 2003)

     FILE 'REGISTRY' ENTERED AT 10:07:33 ON 18 JUN 2003
                E VERAPAMIL
L1             30 S E3-E5
                E VERAPAMIL/CN
L2              1 S E3
                E IODOAMPHETAMINE
L3              9 S E3
                E IODOAMPHETAMINE/CN

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, EMBASE' ENTERED AT 10:08:46 ON
     18 JUN 2003

=> s l1 or l2
L4         75155 L1 OR L2

=> s l4 and l3
L5             6 L4 AND L3

=> dup rem l5
```

PROCESSING COMPLETED FOR L5
L6 6 DUP REM L5 (0 DUPLICATES REMOVED)

=> d ibib ab 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002017144 EMBASE
TITLE: Progress in clinical neurosciences: The evidence for ALS as
a multisystems disorder of limited phenotypic expression.
AUTHOR: Strong M.J.
CORPORATE SOURCE: M.J. Strong, University Campus, London Health Sciences Centre, 339 Windermere Road, London, Ont. N6A 5A5, Canada
SOURCE: Canadian Journal of Neurological Sciences, (2001) 28/4 (283-298).
Refs: 222
ISSN: 0317-1671 CODEN: CJNSA2
COUNTRY: Canada
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB Traditionally, amyotrophic lateral sclerosis (ALS) is considered to be a unique neurodegeneration disorder in which motor neurons are selectively vulnerable to a single disease process. Our current understanding of ALS, however, suggests that this is far too limited an approach. While motor neuron degeneration remains the central component to this process, there is considerable phenotypic variability including broad ranges in survivorship and the presence or absence of cognitive impairment. The number of familial variants of ALS for which unique genetic linkage has been identified is increasing, attesting further to the biological heterogeneity of the disorder. At the cellular level, derangements in cytoskeletal protein and glutamate metabolism, mitochondrial function, and
in glial interactions are clearly evident. When considered in this fashion, ALS can be justifiably considered a disorder of multiple biological processes sharing in common the degeneration of motor neurons.

L6 ANSWER 2 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95127413 EMBASE
DOCUMENT NUMBER: 1995127413
TITLE: Persistent positive visual phenomena in migraine.
AUTHOR: Liu G.T.; Schatz N.J.; Galetta S.L.; Volpe N.J.; Skobieranda F.; Kosmorsky G.S.
CORPORATE SOURCE: Division of Neuro-Ophthalmology, Department of Neurology, Hospital of Univ. of Pennsylvania, 3400 Spruce Street,Philadelphia, PA 19104, United States
SOURCE: Neurology, (1995) 45/4 (664-668).
ISSN: 0028-3878 CODEN: NEURAI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
012 Ophthalmology
023 Nuclear Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Ten patients with migraine developed persistent positive visual phenomena lasting months to years. The complaints were similar in their simplicity and involvement of the entire visual field and usually consisted of diffuse small particles such as TV static, snow, lines of ants, dots, and rain. Neurologic and ophthalmologic examinations were normal, and EEGs were normal in eight of eight patients tested. MRI was normal in all patients except one who had nonspecific biparietal white matter lesions and another with a small venous angioma. Treatment of this unusual complication of migraine was unsuccessful.

L6 ANSWER 3 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94007116 EMBASE
DOCUMENT NUMBER: 1994007116
TITLE: Identification of binding sites for SR 46349B, a 5-hydroxytryptamine2 receptor antagonist, in rodent brain.
AUTHOR: Rinaldi-Carmona M.; Congy C.; Pointeau P.; Vidal H.; Breliere J.-C.; Le Fur G.
CORPORATE SOURCE: Sanofi Recherche, 371 Rue du Professeur Blayac,F-34184 Montpellier Cedex 04, France
SOURCE: Life Sciences, (1994) 54/2 (119-127).
ISSN: 0024-3205 CODEN: LIFSAK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB SR 46349B belongs to a new class of compounds (propenone oxime ether derivative) that inhibit 5-hydroxytryptamine (HT)2 receptors in vitro and in vivo. (3H) SR 46349B has been shown to bind with high affinity (K(d) = 1.20 nM) to a single class of sites in rat prefrontal cortical membranes. The maximum binding capacity (B(max) = 0.262 pmol/mg of protein) is similar to that found for other classes of 5-HT2 receptor antagonists. Although the highest density of specific (3H) SR 46349B binding was found in cortex tissue, specific binding was also detectable in other brain areas. Among various receptor or channel ligands [including .alpha. or .beta. adrenergic, dopamine (D1 or D2), histamine (H1 or H2), 5-HT sublcasses (5-HT1, 5-HT3), muscarinic and Na+ Ca2+ channel blockers] only 5-HT2 receptor effectors were able to displace (3H) SR 46349B. In addition, thye type of inhibition exerted by known 5-HT2 receptor antagonists such as ketanserin and ritanserin was investigated by saturation studies. In vivo, (3H) SR 46349B bound predominantly in mouse brain regions containing 5-HT2 receptors. This binding was displaced by SR
46349B, ketanserin and ritanserin following oral administration. From these results we suggest that SR 46349B in its triated form is a useful tool to label the 5-HT2 receptor in vitro and in vivo.

L6 ANSWER 4 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93180902 EMBASE
DOCUMENT NUMBER: 1993180902
TITLE: Potassium transport at the blood-brain and blood-CSF barriers.
AUTHOR: Keep R.F.; Xiang J.; Betz A.L.
CORPORATE SOURCE: Department of Surgery, University of Michigan,Ann Arbor, MI
48109-0532, United States
SOURCE: Advances in Experimental Medicine and Biology, (1993) 331/-
(43-54).
CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Figure 5 gives a summary of K transporters at the BBB based on the availale evidence. It appears that the cerebral endothelial cells have an array of potassium channels, although the degree to which each is open under physiological conditions is uncertain. Different channels are present on the luminal and abluminal membranes, and the opening and closing of these channels may allow modulation of the brain K influx and efflux rates and play a role in brain K homeostasis. These channels may also play a role in hyperosmotic brain volume regulation of the endothelial cell itself. The nature of fluid transport at the BBB remains to be fully elucidated, with the presence of a Na/K/2Cl co-transporter being uncertain. The abluminal inwardly-rectifying channel may act as a leak pathway to allow modulation of fluid secretion by the Na/K ATPase without altering the K concentration of that fluid. Finally, there is some
evidence that K transport at the BBB is under hormonal and neuronal control. The cerebral capillaries possess receptors for many of the hormones present in blood and brain.

L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:462824 CAPLUS
DOCUMENT NUMBER: 117:62824
TITLE: m-Trifluoromethylphenylpiperazine and m-chlorophenylpiperazine-induced hypothermia in mice is reversed by tricyclic antidepressants and other drugs
AUTHOR(S): Volterra, Giovanna; Cutrufo, Corrado; Lecci, Alessandro
CORPORATE SOURCE: Pharmacol. Res. Div., A. Menarini Farm. S.r.l., Florence, 50131, Italy
SOURCE: European Neuropsychopharmacology (1991), 1(4), 519-28. CODEN: EURNE8; ISSN: 0924-977X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many antidepressants reverse arylpiperazine-induced hypothermia after acute treatment by a mechanism that does not seem to implicate monoamine uptake inhibition. Activity is found in reversing 1-(m-trifluoromethylphenyl)piperazine (TFMPP)-induced hypothermia by desipramine 5 and 10 mg/kg and not by maprotiline 10 and 20 mg/kg. Clomipramine and fluxoetine with comparable serotonin uptake blocking potential do not have comparable TFMPP-reversing effects. A dibenzothiadiazepine compd. (IM/P/3/4), hypothesized to have antidepressant activity though devoid of uptake blocking properties, was active at 10 and 20 mg/kg. Other classes of tricyclics such as neuroleptics (clozapine 5 and 10 mg/kg) and chlorpromazine (2 and 10 mg/kg) and the H1 antihistamines, promethazine (20 mg/kg) and cyproheptadine (10 mg/kg) are active, as well as the calcium antagonists nifedipine (10 mg/kg) and verapamil (10 mg/kg). The authors hypothesize that properties other than monoamine-uptake block which these compds. share (such as calcium-uptake inhibition) could be involved. Activity was also seen with the 5-HT1A agonists 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT, at 0.05 and 0.25 mg/kg), and 5-methoxy-N,N-dimethyltryptamine (5-MeODMT at 3 mg/kg) as well as with the muscarinic agonist oxotremorine (0.1 mg/kg). Antidepressants and calcium channel antagonists also reversed m-chlorophenylpiperazine-induced hypothermia.

L6 ANSWER 6 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91134187 EMBASE
DOCUMENT NUMBER: 1991134187
TITLE: Receptor pharmacology of MDMA and related hallucinogens.
AUTHOR: Teitler M.; Leonhardt S.; Appel N.M.; De Souza E.B.; Glennon R.A.
CORPORATE SOURCE: Dept. Pharmacology/Toxicology, Albany Medical College,Albany, NY 12208, United States
SOURCE: Annals of the New York Academy of Sciences, (1990) 600/- (626-639). ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 032 Psychiatry
040 Drug Dependence, Alcohol Abuse and Alcoholism
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The data presented herein appear to strongly implicate the brain 5HT2 receptor as the site-of-action of the hallucinogenic PIAs and LSD. If so, this discovery represents a major step in understanding the molecular pharmacology of hallucinogenic drugs. Using radioactive hallucinogenic drugs, detailed properties of brain 5HT2 receptors indicating the interaction of 5HT2 receptors with GTP-binding proteins have been revealed. Autoradiographic studies have revealed an extensive cortical distribution of brain 5HT2 receptors; these studies have also suggested that the PIAs may be 5HT(1C) agonists. Radiolabeling studies in conjunction with drug discrimination studies indicate that MDMA is apparently ''amphetamine-like'' and not ''LSD-like'' while MDA is apparently both ''LSD-like'' and ''amphetamine-like.'' However MDMA does appear to possess the potential to act as a 5HT2 agonist at high dosages.

```
=> l4 and plasm?
L4 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l4 and plasm?
L7        6169 L4 AND PLASM?

=> s l7 and (plasma(w)protein?)
L8         220 L7 AND (PLASMA(W) PROTEIN?)

=> s l8 and (administ? or in vivo)
L9         139 L8 AND (ADMINIST? OR IN VIVO)

=> s l9 and (radiolabel? or radionuclid? or radiodiagn? or radiother? or label? or
radioactiv?)
L10         21 L9 AND (RADIOLABEL? OR RADIONUCLID? OR RADIODIAGN? OR RADIOTHER
               ? OR LABEL? OR RADIOACTIV?)

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11          16 DUP REM L10 (5 DUPLICATES REMOVED)

=> s l6 nog l11
MISSING OPERATOR L6 NOG
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l6 not l10
L12           6 L6 NOT L10

=> s l11 not l6
L13          16 L11 NOT L6

=> d ibib ab 1-
YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y
```

L13 ANSWER 1 OF 16 MEDLINE
ACCESSION NUMBER: 95254452 MEDLINE
DOCUMENT NUMBER: 95254452 PubMed ID: 7736407
TITLE: Modulation of P-glycoprotein activity by estramustine is limited by binding to **plasma proteins**.
AUTHOR: Smith C D; Zilfou J T; Zhang X; Hudes G R; Tew K D
CORPORATE SOURCE: Department of Pharmacology, Fox Chase Cancer Center, Philadelphia, PA 19111, USA.
SOURCE: CANCER, (1995 May 15) 75 (10) 2597-604.
Journal code: 0374236. ISSN: 0008-543X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950615
Last Updated on STN: 19970203
Entered Medline: 19950608

AB BACKGROUND. Estramustine previously has been shown to interact with P-glycoprotein and to restore intracellular accumulation of vinblastine and paclitaxel in cells overexpressing this drug transporter. However, the ability of estramustine to potentiate the cytotoxicities of several drugs was less than that expected. To resolve this apparent discordance, the authors examined the effects of serum on the actions of estramustine. METHODS. The cytotoxicities of anticancer drugs with or without estramustine or verapamil toward MCF-7 breast carcinoma cells and a P-glycoprotein-overexpressing subline MCF-7/ADR were determined using the sulforhodamine-binding assay. The extent of intracellular accumulation of [3H]vinblastine and [3H]paclitaxel was determined for each using standard methods, and the binding of **radiolabeled** drugs to **plasma proteins** was characterized by equilibrium dialysis. RESULTS. Without serum, the sensitivities of MCF-7/ADR cells to several P-glycoprotein-transported drugs were increased by estramustine and verapamil. Conversely, when the cells were treated with a 10% serum, the cytotoxicities of these drugs were increased by verapamil, but not by estramustine. Without serum, intracellular accumulation of [3H]vinblastine and [3H]paclitaxel by MCF-7/ADR cells was increased markedly by verapamil and estramustine; however, serum suppressed the effects of estramustine much more strongly than those of verapamil. Equilibrium dialysis experiments demonstrated that [3H]estramustine binds to **plasma proteins**, predominantly albumin, whereas [3H]paclitaxel binds to albumin and alpha 1-acid-glycoprotein, and [3H]vinblastine binds predominantly to alpha 1-acid-glycoprotein. CONCLUSION. Although estramustine can bind to P-glycoprotein, its effectiveness as a reversing agent in **vivo** likely is limited by binding to **plasma proteins**.

L13 ANSWER 2 OF 16 MEDLINE
ACCESSION NUMBER: 85290010 MEDLINE
DOCUMENT NUMBER: 85290010 PubMed ID: 3875635
TITLE: **Plasma protein** binding of bepridil.
AUTHOR: Pritchard J F; McKown L A; Dvorchik B H; O'Neill P J
SOURCE: JOURNAL OF CLINICAL PHARMACOLOGY, (1985 Jul-Aug) 25 (5) 347-53.
Journal code: 0366372. ISSN: 0091-2700.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198509
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850927

AB The binding of the calcium-channel blocking agent, bepridil HCl (Vascor), to **plasma proteins** was investigated using **radiolabeled** bepridil and equilibrium dialysis. Greater than 99.7% of added bepridil-14C was found to freshly collected human **plasma**. The binding was characterized by a saturable high-affinity site (KD = 32 ng/mL = 87 nM) on alpha1-acid glycoprotein (AAG) or on an AAG-human serum albumin complex and lower affinity binding sites on albumin and other **plasma** macromolecules. Bepridil that is not bound to **plasma proteins** is extensively distributed into erythrocytes as evidenced by a red blood cell to free drug distribution coefficient of 71 +/- 7. Despite this high value, the blood to **plasma** ratio of bepridil averaged only 0.67 in humans, indicating that most of the circulating drug is bound to **plasma proteins**. Bepridil protein binding was not affected by additions of nonesterified fatty acids. Free fractions of bepridil were enhanced by addition of verapamil, nifedipine, diltiazem, disopyramide, and warfarin but only at concentrations above those achieved clinically. Bepridil was also displaced by the plasticizer, tris-(2-butoxyethyl)phosphate. **Plasma** obtained from a small number of angina patients prior to bepridil **administration** showed no differences in ability to bind bepridil compared with **plasma** obtained from healthy subjects.

L13 ANSWER 3 OF 16 MEDLINE
ACCESSION NUMBER: 81232612 MEDLINE
DOCUMENT NUMBER: 81232612 PubMed ID: 7248141
TITLE: Pharmacokinetics, bioavailability and ECG response of verapamil in patients with liver cirrhosis.
AUTHOR: Somogyi A; Albrecht M; Kliems G; Schafer K; Eichelbaum M
SOURCE: BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, (1981 Jul) 12 (1) 51-60.
Journal code: 7503323. ISSN: 0306-5251.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198109
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19810922

AB 1 The pharmacokinetics, bioavailability and ECG response of verapamil was investigated in seven patients with liver cirrhosis and compared with six normal subjects, using stable **labelled** techniques whereby both the intravenous and oral dose are given simultaneously. 2 After intravenous **administration**, **plasma** concentrations were much higher in the patient group such that the total **plasma** clearance was reduced from a mean of 1258 ml/min in normals to 616 ml/min in the patient group (P less than 0.0025). The apparent volume of distribution nearly doubled (6.76 v 12.05 l/kg, P less than 0.025) and the terminal half-life was prolonged four fold (3.7 v 14.2 h, P less than 0.001). 3 Given orally, the peak **plasma** concentration was higher and occurred earlier in the liver cirrhotic patients. The absolute bioavailability more than doubled (22.0% normals v 52.3% liver cirrhotics, P less than 0.001) and apparent oral clearance was reduced to only 20% of normal (6.38 v 1.30 l/min, P less than 0.001). 4 The delta P-R interval in the patient group lagged behind the **plasma** concentration, in contrast to normal subjects. The maximum effect was much greater in the patients (15.4 v 41.6% increase, P less than 0.005) and persisted for a longer period of time. The slope of the **plasma** concentration-response curve was the same as in normals after intravenous **administration**. **Plasma protein** binding remained unchanged. 5 It is recommended that in liver cirrhotic patients the intravenous dose of verapamil be halved and the oral dose decreased by a factor of five in order to prevent untoward effects. As well as a steady-state **plasma** concentration will not be reached until approximately 2 days after the beginning of therapy.

L13 ANSWER 4 OF 16 USPATFULL
ACCESSION NUMBER: 2003:45283 USPATFULL
TITLE: Compositions and methods relating to glucose metabolism, weight control, and food intake
INVENTOR(S): Desir, Gary, Woodbridge, CT, UNITED STATES
Xu, Jianchao, Bethany, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003032595	A1	20030213
APPLICATION INFO.:	US 2002-167528	A1	20020611 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-297547P	20010612 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORGAN, LEWIS & BOCKIUS LLP, 1701 MARKET STREET, PHILADELPHIA, PA, 19103-2921
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Page(s)
LINE COUNT: 2823
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to weight control, control of body fat and food intake, and provides useful methods for treating, inter alia, obesity, diabetes and insulin insensitivity, and conditions, diseases, and disorders relating thereto. The invention also relates to methods of identifying useful compounds relating to weight loss, food intake, diabetes, and obesity, among other things, based on the discovery that inhibiting Kv1.3 activity mediates decreased food intake, weight loss, decreased body fat, increase glucose uptake, and increased insulin sensitivity, among other things.

L13 ANSWER 5 OF 16 USPATFULL
ACCESSION NUMBER: 2003:40407 USPATFULL
TITLE: C-CAM as an angiogenesis inhibitor
INVENTOR(S): Lin, Sue-Hwa, Houston, TX, United States
Luo, Weiping, Pearland, TX, United States
Logothetis, Christopher, Houston, TX, United States
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6517828	B1	20030211
APPLICATION INFO.:	US 2000-580043		20000526 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-136563P	19990528 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Wortman, Donna
ASSISTANT EXAMINER: Rawlings, Stephen L.
LEGAL REPRESENTATIVE: Fulbright & Jaworski, L.L.P.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 3949
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates generally to the fields hyperproliferative
disease and angiogenesis. More particularly, the present invention demonstrates that a C-CAM1 cytoplasmic domain is necessary and sufficient for inhibiting angiogenesis. In particular embodiments, it relates to inhibiting hyperproliferative cell growth by **administering** to a cell a C-CAM1 cytoplasmic domain or an expression construct encoding a C-CAM1 cytoplasmic domain. In other embodiments, angiogenesis is inhibited by **administering** to a subject a C-CAM1 polypeptide or an expression construct encoding a C-CAM1 polypeptide.

L13 ANSWER 6 OF 16 USPATFULL
ACCESSION NUMBER: 2002:116090 USPATFULL
TITLE: Removal of viruses from protein solutions by ultrafiltration
INVENTOR(S): Bernhardt, Dieter, Colbe, GERMANY, FEDERAL REPUBLIC OF
Groner, Albrecht, Seeheim, GERMANY, FEDERAL REPUBLIC OF
Nowak, Thomas, Staufenberg-Mainzlas, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Aventis Behring GmbH, Marburg, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6391657	B1	20020521
	US 2002068368	A1	20020606
APPLICATION INFO.:	US 1996-598264		19960207 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1995-19504211	19950209

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Wortman, Donna C.
LEGAL REPRESENTATIVE: Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 289
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the removal of viruses from aqueous solutions, as a rule protein solutions, by ultrafiltration. This entails the viruses to be removed being increased in size by incubation with a high molecular weight receptor binding thereto, preferably a specific antibody, so that, on the one hand, the separation effect is improved and, on the other hand, a larger pore diameter which can now be chosen for the filters used also makes it possible for smaller viruses to be separated from larger protein molecules present in protein solutions, and, where appropriate, the filtration rate is increased.

L13 ANSWER 7 OF 16 USPATFULL
ACCESSION NUMBER: 2002:32198 USPATFULL
TITLE: Method and apparatus for assaying a drug candidate to estimate a pharmacokinetic parameter associated therewith
INVENTOR(S): Hamalainen, Markku, Uppsala, SWEDEN
Karlsson, Robert, Uppsala, SWEDEN
Lofas, Stefan, Uppsala, SWEDEN

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002019019	A1	20020214
APPLICATION INFO.:	US 2001-921496	A1	20010803 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-336865, filed on 18 Jun 1999, ABANDONED		

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
NUMBER OF CLAIMS: 47
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method and apparatus for assaying a drug candidate with a biosensor having one or more sensing surface-bound biomolecules associated therewith are disclosed. The method comprises the steps of measuring the
binding interaction between the drug candidate and the one or more sensing surface-bound biomolecules of the biosensor to obtain an estimate of at least one binding interaction parameter of the drug candidate, and then comparing the estimated binding interaction parameter against a mathematical expression correlated from binding interaction data associated with known drug compounds to determine an estimate of at least pharmacokinetic parameter of absorption, distribution, metabolism, or excretion (ADME) that is related to the drug candidate. The present invention allows for the simultaneous measurement of different pharmacokinetic parameters of the drug candidate, as well as an indication of the drug candidate's solubility, by use of a single analytical instrument. The pharmacokinetic data may be represented as a ADME characterization profile; such ADME profiles are of great utility for purposes of drug screening and lead optimization.

L13 ANSWER 8 OF 16 USPATFULL
ACCESSION NUMBER: 2002:27445 USPATFULL
TITLE: Flavopiridol drug combinations and methods with reduced
side effects
INVENTOR(S): Ratain, Mark J., Chicago, IL, UNITED STATES
Innocenti, Federico, Chicago, IL, UNITED STATES
Iyer, Lalitha, Chicago, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002016293	A1	20020207
APPLICATION INFO.:	US 2001-835082	A1	20010412 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-553829, filed on 21 Apr 2000, PENDING		

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gina N. Shishima, Fulbright & Jaworski L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701
NUMBER OF CLAIMS: 99
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 5370
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods, formulations and kits to reduce the toxicity of flavopiridol and analogs thereof. Disclosed are therapeutics
and treatment methods employing such drugs in combination with agents that increase conjugative enzyme activity or glucuronosyltransferase activity, and agents that decrease biliary transport protein activity, such as cyclosporine A, the resultant effects of which are to decrease the significant side effects previously associated with treatment using these drugs. The invention also characterizes specific isoforms of glucuronyltransferase enzymes involved in glucuronidation of flavopiridols and their analogs.

L13 ANSWER 9 OF 16 USPATFULL
ACCESSION NUMBER: 2001:4475 USPATFULL
TITLE: Methods for releasing a ligand from a complex
INVENTOR(S): Staples, Mark A., San Jose, CA, United States
Haley, Carolyn J., Morgan Hill, CA, United States
Parrish, Richard F., San Jose, CA, United States
Zmolek, Wesley W., Freemont, CA, United States
PATENT ASSIGNEE(S): Dade Behring Marburg GmbH, Marburg, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6171801	B1	20010109
APPLICATION INFO.:	US 1997-896244		19970717 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-22133P	19960718 (60)

DOCUMENT TYPE: Patent
FILE SEGMENT: Granted
PRIMARY EXAMINER: Housel, James C.
ASSISTANT EXAMINER: Devi, S.
LEGAL REPRESENTATIVE: Lowen, Cara Z.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 1370
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB One aspect of the present invention relates to a method for releasing a ligand from a complex thereof. The method comprises contacting a medium suspected of containing such complex with an effective amount of a compound effective in releasing the ligand. Another aspect of the present invention is an improvement in a method for the determination of an analyte that is a member of a specific binding pair in a sample suspected of containing such analyte. The method comprises the steps of (a) providing in an assay medium the sample and a binding partner for the analyte and (b) detecting the binding of the binding partner to the analyte. The improvement comprises including in the assay medium a compound of the invention in an amount sufficient to enhance the accuracy of the determination. The invention has particular application to a method for releasing mycophenolic acid from a complex thereof. The method provides an improvement in a method for the determination of mycophenolic acid in a sample suspected of containing mycophenolic acid.
The present invention also provides assay reagents as well as packaged kits useful for performing the methods of the invention.

L13 ANSWER 10 OF 16 USPATFULL
ACCESSION NUMBER: 2000:91720 USPATFULL
TITLE: Sphingoglycolipids as markers for multidrug resistant cancers
INVENTOR(S): Cabot, Myles, Santa Monica, CA, United States
PATENT ASSIGNEE(S): John Wayne Cancer Institute, Santa Monica, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6090565		20000718
APPLICATION INFO.:	US 1997-964656		19971105 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1996-636513, filed on 19 Apr 1996, now patented, Pat. No. US 5885786
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Caputa, Anthony C.
ASSISTANT EXAMINER: Weatherspoon, John K.
LEGAL REPRESENTATIVE: Arnold, White & Durkee
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 24 Drawing Page(s)
LINE COUNT: 2938
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention involves the identification of sphingoglycolipid species that are indicative of multidrug resistance in certain types of cells, including cancer cells. The association of multidrug resistance with the expression of certain sphingoglycolipids provides a new method for identifying multidrug resistant cancers. In addition, it has been determined that reducing the levels of certain sphingoglycolipids results in enhanced chemosensitivity of drug resistant cancer cells. This offers the opportunity to develop new treatments for multidrug resistant cancers.

L13 ANSWER 11 OF 16 USPATFULL
ACCESSION NUMBER: 1999:36909 USPATFULL
TITLE: Methods for screening of substances for inhibition of multidrug resistance
INVENTOR(S): Cabot, Myles, Santa Monica, CA, United States
PATENT ASSIGNEE(S): John Wayne Cancer Institute, Santa Monica, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5885786		19990323
APPLICATION INFO.:	US 1996-636513		19960419 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Duffy, Patricia
LEGAL REPRESENTATIVE: Arnold, White & Durkee
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 32 Drawing Figure(s); 24 Drawing Page(s)
LINE COUNT: 2921
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides for the screening of candidate substances to identify active compounds that inhibit multidrug resistance (MDR). The expression of glucosylceramides has been determined to be a marker of MDR. By measuring glucosylceramide expression in cells exhibiting MDR, and the reduction in glucosylceramide levels in the presence of a candidate substance, the present invention provides for the identification of MDR inhibitory compounds.

L13 ANSWER 12 OF 16 USPATFULL
ACCESSION NUMBER: 1998:88829 USPATFULL
TITLE: Camptothecin drug combinations and methods with reduced side effects
INVENTOR(S): Ratain, Mark J., Chicago, IL, United States
Gupta, Elora, Chicago, IL, United States
PATENT ASSIGNEE(S): Arch Development Corporation, Chicago, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5786344		19980728
APPLICATION INFO.:	US 1995-423641		19950417 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-271278, filed on 5 Jul 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Nazario-Gonzalez, Porfirio
LEGAL REPRESENTATIVE: Arnold, White & Durkee
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1,29,30
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 4037
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods and combination formulations and kits to reduce the toxicity of camptothecin drugs, such as irinotecan (CPT-11). Disclosed are therapeutics and treatment methods employing such drugs in combination with agents that increase conjugative enzyme activity or glucuronosyltransferase activity, and agents that decrease biliary transport protein activity, such as cyclosporine A, the resultant effects of which are to decrease the significant side effects previously associated with treatment using these drugs.

L13 ANSWER 13 OF 16 USPATFULL
ACCESSION NUMBER: 1998:51572 USPATFULL
TITLE: Method to improve the biological and antiviral activity of protease inhibitors
INVENTOR(S): Sommadossi, Jean-Pierre, Birmingham, AL, United States
Schinazi, Raymond F., 1524 Regency Walk Dr., Decatur, GA, United States 30033
PATENT ASSIGNEE(S): Schinazi, Raymond F., Decatur, GA, United States (U.S. individual)
University of Alabama at Birmingham, Birmingham, AL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5750493		19980512
APPLICATION INFO.:	US 1995-521474		19950830 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ketter, James
ASSISTANT EXAMINER: Brusca, John S.
LEGAL REPRESENTATIVE: Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
NUMBER OF CLAIMS: 39
EXEMPLARY CLAIM: 1
LINE COUNT: 917
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for improving the cellular uptake of protease inhibitors (e.g., HIV protease inhibitor), alone or in the presence of one or more additional therapeutic agents, in protease inhibitor-based therapies, involving **administration** of one or more AAG-binding compounds, such as macrolide or lincosamide antibiotics, which have sufficient binding affinity for AAG to competitively bind AAG in the presence of the protease inhibitor.

L13 ANSWER 14 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001306014 EMBASE
TITLE: Effect of mdr1a p-glycoprotein gene disruption, gender, and substrate concentration on brain uptake of selected compounds.
AUTHOR: Dagenais C.; Zong J.; Ducharme J.; Pollack G.M.
CORPORATE SOURCE: G.M. Pollack, Division of Drug Delivery, School of Pharmacy, University of North Carolina, Chapel Hill, NC 27599-7360, United States. gary_pollack@unc.edu
SOURCE: Pharmaceutical Research, (2001) 18/7 (957-963).
Refs: 30
ISSN: 0724-8741 CODEN: PHREEB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose. This study assessed the influence of mdr1a P-glycoprotein (P-gp) gene disruption, gender and concentration on initial brain uptake clearance (Cl(up)) of morphine, quinidine and verapamil. Methods. Cl(up) of **radiolabeled** substrates was determined in P-gp-competent and deficient [mdr1a(-/-)] mice by in situ brain perfusion. Brain: **plasma** distribution of substrates after i.v. **administration** was determined in both strains. Results. Genetic disruption of mdr1a P-gp resulted in 1.3-, 6.6- and 14-fold increases in Cl(up) for morphine, verapamil and quinidine, respectively. With the exception of small differences for verapamil, gender did not affect Cl(up). Saturable transport of verapamil and quinidine was observed only in P-gp-competent mice, with apparent IC(50) values for efflux of 8.6 .+-. 2.3 .mu.M and 36 .+-. 2 .mu.M, respectively. Verapamil Cl(up) was .apprx.50% higher in mdr1a(+/-) vs. mdr1a(+/+) mice; no such difference was observed for quinidine. In P-gp-competent mice, uptake of verapamil and quinidine was unaffected by organic vehicles. **Plasma** decreased VER Cl(up) to a greater extent in the presence of P-gp. The influence of P-gp in situ was lower than, but correlated with, the effect in **vivo**. Conclusions. P-gp decreases Cl(up) of morphine, verapamil and quinidine in situ with little or no influence of gender, but this effect cannot fully account for the effects of P-gp in **vivo**. P-gp is the only saturable transport mechanism for verapamil and quinidine at the murine blood-brain barrier. The influence of protein binding on Cl(up) may be enhanced by P-gp-mediated efflux.

L13 ANSWER 15 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97289611 EMBASE
DOCUMENT NUMBER: 1997289611
TITLE: Updates of cabergoline and azelastine nasal spray.
AUTHOR: Levien T.; Baker D.E.
CORPORATE SOURCE: D.E. Baker, Drug Information Center, Professor of Pharmacy Practice, Washington State University, 601 West First Avenue, Spokane, WA 99204-0399, United States
SOURCE: Hospital Pharmacy, (1997) 32/9 (1252-1270).
Refs: 29
ISSN: 0018-5787 CODEN: HOPHAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
011 Otorhinolaryngology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L13 ANSWER 16 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93359875 EMBASE
DOCUMENT NUMBER: 1993359875
TITLE: Metabolic fate of AA-2414, a new thromboxane A2 receptor antagonist, in rats, guinea-pigs, dogs, and monkeys.
AUTHOR: Miwa K.; Imamoto T.; Ikeda M.; Hagihara K.; Yanaga Y.; Yoshida K.; Yoshimura Y.; Tanayama S.
SOURCE: Japanese Pharmacology and Therapeutics, (1993) 21/SUPPL. 7 (201-228).
ISSN: 0386-3603 CODEN: YACHDS
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
023 Nuclear Medicine
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB After oral dosing of 14C-**labeled** AA-2414 ([14C] AA-2414), 37, 74, 59, and 92% of the **radioactivity** were absorbed in rats, guinea-pigs, dogs, and monkeys, respectively. The bioavailability of the compound was 35% in rats, 75% in guinea-pigs, 48% in dogs, and 89% in monkeys. The **plasma** level of AA- 2414 in rats reached a peak 15 min after dosing and then decreased biphasically with apparent half-lives of 0.6 and 2.7 h. In guinea-pigs, the **plasma** level attained a plateau at 30 min, which persisted until 8 h, and then decreased with an apparent half-life of 9.3 h. In dogs, the **plasma** level of AA-2414 reached a peak 15 min post dosing, and declined biphasically with apparent half-lives of 0.8 and 6.1 h. In monkeys, peak **plasma** level of AA- 2414 reached at 1 h, and apparent elimination half-lives were 3.1 and 48 h. Circulating major component in these animals was unchanged AA-2414. Sulfate conjugate of reduced AA-2414 (hydroquinone form of AA-2414) in rats, guinea- pigs, and dogs, and glucuronide of that in monkeys were also major components. The pharmacokinetics of AA-2414 in rats and monkeys were linear in a dose range of 5 to 20 mg/kg and 5 to 100 mg/kg, respectively. [14C] AA-2414 was widely distributed throughout the bodies of rats and guinea-pigs after oral dosing, with relatively high concentrations found in the gastrointestinal tract, liver, and kidney. AA-2414 and its metabolites transferred into rat fetus and milk. The major component in tissues was unchanged AA-2414. [14C] AA-2414 and its metabolites were extensively bound to **plasma proteins** of rats, guinea-pigs, dogs, and monkeys, and serum proteins of humans. No protein binding interaction between AA-2414 and warfarin, theophylline, isoproterenol, diazepam, propranolol, verapamil, and diphenylhydantoin was observed in human serum. However, non-protein binding concentration of AA-2414 in human serum tended to increase with increasing concentration of aspirin. Following oral **administration**, AA-2414 and its metabolites were excreted predominantly in feces via hepatobiliary route in rats and dogs. In guinea-pigs and monkeys, a large amount of those was excreted in urine. No appreciable amount of [14C] AA-2414 was accumulated in the bodies of guinea-pigs and monkeys on repeated medication. Daily oral **administration** of AA-2414 to rats resulted in a weak inhibition of microsomal aminopyrine N-demethylase activity.

L13 ANSWER 16 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. (Continued)

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                                                 ENTRY    SESSION
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LAST RELOADED: Jun 13, 2003 (20030613/UP).

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FULL ESTIMATED COST                               2.88     100.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
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     FILE 'REGISTRY' ENTERED AT 10:07:33 ON 18 JUN 2003
                E VERAPAMIL
L1             30 S E3-E5
                E VERAPAMIL/CN
L2              1 S E3
                E IODOAMPHETAMINE
L3              9 S E3
                E IODOAMPHETAMINE/CN

     FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, EMBASE' ENTERED AT 10:08:46 ON
     18 JUN 2003
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L4        75155 S L1 OR L2
L5            6 S L4 AND L3
L6            6 DUP REM L5 (0 DUPLICATES REMOVED)
L7         6169 S L4 AND PLASM?
L8          220 S L7 AND (PLASMA(W)PROTEIN?)
L9          139 S L8 AND (ADMINIST? OR IN VIVO)
L10          21 S L9 AND (RADIOLABEL? OR RADIONUCLID? OR RADIODIAGN? OR RADIOT
L11          16 DUP REM L10 (5 DUPLICATES REMOVED)
L12           6 S L6 NOT L10
L13          16 S L11 NOT L6

     FILE 'STNGUIDE' ENTERED AT 10:14:52 ON 18 JUN 2003

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